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(54) LIQUID SUCTION EXAMINATION METHOD AND DISPENSATION APPARATUS DRIVING-CONTROLLED BY THE SAME

(57) There are provided an entire new method for sucking/determining a liquid and a pipetting device driven and controlled by the method in which a liquid level of a liquid sucked by a nozzle, contamination of a liquid with foreign matters, or an interface of a liquid with another liquid having different color are determined by detecting fluctuation of a light obtained from a liquid accommodated in a vessel with a nozzle provided in the nozzle for sucking the liquid, and a liquid level, contamination of a liquid with foreign matters, or an interface of a liquid with another liquid having a different color can be detected with extremely high-sensitivity without being affected by a wavy liquid level by monitoring a pipetting chip or an opening section at a tip of a chip in a cleaning system as if to visually check the other opening section of a tunnel from one side thereof.

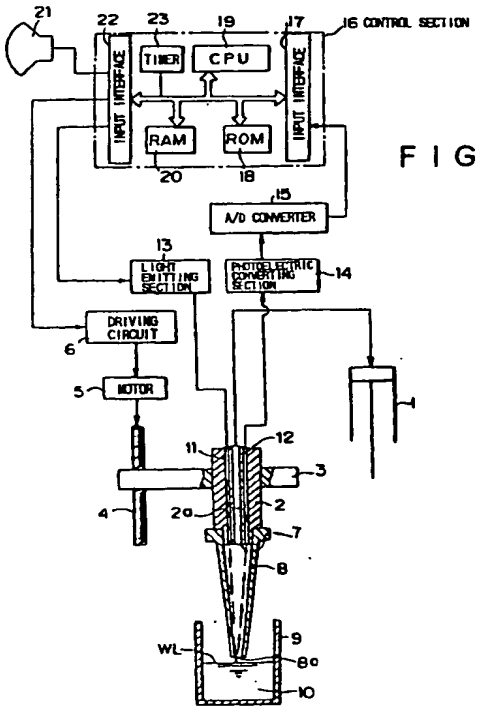

FIG. 1

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Description

TECHNICAL FIELD

The present invention relates to an entirely new method for sucking/determining a liquid and a pipetting device driven and controlled according to the method, and more particularly to a method for sucking/determining a liquid in which driving required for upward/downward movement of a nozzle for sucking a liquid such as a sample for a blood serum and a reagent as well as for pipetting a liquid to cylinders each for sucking and discharging the liquid is accurately controlled, so that a liquid level and a sucking rate of a liquid by the nozzle, and contamination of foreign matters therein such as bubbles or fibrins or the like in the liquid can accurately be detected, as well as to a pipetting device driven and controlled according to the method.

BACKGROUND ART

Generally, important matters required for enhancing pipetting precision are to detect a level of a blood serum sample and a reagent or similar liquid, to measure a pipetting rate thereof, to measure an absolute sucking rate thereof, to adhere the liquid to the outside of the nozzle, and to detect contamination thereof by foreign matters such as bubbles and fibrins.

For this reason, conventionally, a method, has been employed, in which an electrode is immersed in the liquid together with the nozzle and the liquid level is detected according to a conductive state with the electrode so that an inserting rate (distance) of the nozzle to the liquid is controlled, but in the case of this method, the electrode must be immersed into the liquid, so that the electrode must be washed after each measurement thereof to prevent cross contamination, and as a result, there have been such problems as that a device becomes complicated, and that size and cost of the device increase.

Then, recently a method of detecting a liquid level using a pressure sensor was proposed. In this method, a sucking pressure of the nozzle when a vapor is sucked is different from that when a liquid is sucked, so that the liquid level is detected by detecting the difference between the pressures, whereby an inserting rate (distance) of the nozzle to the liquid is controlled, and for this reason only the nozzle is contacted with the liquid, and the method has such advantages as that a cleaning function is not required, which makes it possible to simplify the device as well as to reduce the costs.

However, the method of detecting a liquid level using a pressure sensor has several problems such as that the resolution is low and the sensitivity is not high, and also that the method is easily affected by an atmospheric pressure as well as by pressure change due to the sucked air, and also affected by vibrations generated due to upward/downward movement of the nozzle as well as by a noise of the pipetting device itself or a change of a voltage, and for this reason malfunction thereof occurs quite often, and the reliability thereof as a measuring means is quite low.

An optical liquid level detecting means is far more effective as a means to solve the problems as described above, and various means in which both an optical fiber for irradiating a light therethrough and an optical fiber for receiving a light are provided outside the nozzle for receiving a reflected light from a liquid level with the optical fiber for receiving a light to detect the level thereby are proposed for the liquid level detecting methods based on the conventional technology.

However, in the liquid level detecting means using a light for detecting a liquid level based on the conventional technology, in which both a fiber for irradiating a light therethrough and an optical fiber for receiving a light are provided outside the nozzle for catching a reflected light from a liquid level with the optical fiber for receiving a light to detect the level thereby, these fibers have to be inserted in parallel to each other together with the nozzle into a vessel for a liquid, and for this reason it can not be denied that the method has a possibility of cross contamination caused by the fiber contacting with the liquid adhered to the wall surface of the vessel for a liquid, and also the amount of light caught by the optical fiber for receiving a light is extremely small, which makes it difficult to accurately detect a liquid level, and in addition the extremely minute control is required, which is difficult because there also occur some cases where a timing for receiving the reflected light is shifted or a light can not be received by the fact that the liquid level becomes slightly wavy due to vibrations of the device.

The present invention was made to solve the problems as described above, and it is an object of the present invention to provide an entirely new method of sucking/determining a liquid, including, for instance, detection of a liquid level in which a light receiving body is provided in a nozzle, and fluctuation of a light in a disposable chip such as a pipetting chip and in an opening section at the tip of a chip in a cleaning system are detected thereby from the side of nozzle under circumstances as if to see the other opening section from one side of a tunnel, so that it is possible to extremely sensitively detect a liquid level, contamination by foreign matters therein, or an interface between liquids each having a different color without being affected by the wavy liquid level, as well as to provide a pipetting device driven and controlled according to the method. Namely, a basic principle of the present invention is characterized in that the various types of detecting operation are carried out by catching a moment as if a light instantly changed shows fluctuation in a flash when near-by substance in a space cut off from the outside of the environment is changed in a way, for instance, from vapor to liquid.

DISCLOSURE OF INVENTION

To achieve the object as described above, in the method of sucking/determining a liquid according to the present invention, it is essential to detect variations of lights caused by a liquid accommodated in the vessel with the nozzle for sucking the liquid.

In the present invention, a disposable chip or a chip in a cleaning system is attached to a lower edge section of the nozzle, and the nozzle detects a liquid level by receiving fluctuation of a light close to the disposable chip or to an opening section at a tip of the chip in a cleaning system, for instance, a light reflected from the liquid surface.

Furthermore, in the present invention, not only the liquid level is detected, but also a liquid is filled in the disposable chip or the chip in a cleaning system detachably attached to the nozzle, a light is passed through the liquid in the disposable chip or the chip in a cleaning system, and a change of a light amount of the sucked liquid is detected, so that, for instance, a suction rate of the liquid, transparency thereof, contamination by bubbles therein, clogging and a state that water has been exhausted are determined.

And furthermore, in the present invention, fluctuation of a light wave length can be detected and a change of color is checked by the nozzle, whereby a liquid level can also be detected. The color change can be detected according to the nozzle to detect a color of the colored vessel accommodating a liquid therein through the liquid, or according to the nozzle to detect a color of a rack or a color of a holder in which a transparent vessel accommodating a liquid therein is vertically provided, through the liquid. It is needless to say that detection of color change herein includes detecting an interface on which layers are separated by identifying a color of a blood clot or a blood coagulant in a process, for instance, in which the nozzle is moving downward while sucking a blood serum.

In the present invention, the light is not limited to a case of a light which is directly received from the disposable chip or from the opening section of the tip on the chip in a cleaning system attached to the nozzle, and, for instance, a light may be irradiated or received through a transparent disposable chip or a chip in a cleaning system.

In the present invention, it is desirable that the nozzle itself is formed with a light transmitting material in a tubular form, or only the lower edge section thereof is formed with the light transparent material, or a flux of optical fibers are provided therein.

In this case, it is desirable that a lens body is provided in the tip section of a disposable chip or a chip in a cleaning system in the nozzle, for instance, in a slightly lower side than the opening section in the tip of the disposable chip or the lower edge thereof, so that the lens can be focused at a position where fluctuation of an amount of received light can be checked with high-precision. The lens may be used depending on conditions of a form or a length of a chip, diameter of an opening section, light-proof property or the like, and in this case, the lens may be provided in any of a light irradiating section and/or a light receiving section, and a concave lens may be used as well as a convex lens, or a plurality of concave and convex lenses may be combined to be used.

In the present invention, a light is supplied to a liquid accommodated in a vessel through a nozzle itself or a fiber for light irradiation and a light receiving fiber each provided inside the nozzle, or is supplied from the outside of the nozzle.

A supply of a light from the outside of the nozzle includes irradiation of a light from the outside of a transparent vessel for a liquid to a liquid, or irradiation of a light to a liquid through a disposable chip or a chip in a cleaning system in addition to irradiation of a light from an optical fiber provided near the outside of the nozzle to a liquid. It is needless to say that, irradiation of a light is not limited to a case where a light is irradiated continuously, but a light may be irradiated by blinking it at certain time intervals.

Data obtained by the method for sucking/determining a liquid having the construction as described above is preferably used as data for controlling a pipetting device in which driving required for pipetting a liquid to cylinders for moving upward/downward the nozzle as well as for sucking/discharging a liquid is controlled.

BRIEF DESCRIPTION OF DRAWINGS

Fig. 1 is an explanatory view showing schematic configuration of a pipetting device according to a first embodiment of the present invention; Fig. 2 is an explanatory view showing schematic configuration of a pipetting device according to a second embodiment of the present invention; Fig. 3 is an explanatory view showing schematic configuration of a pipetting device according to a third embodiment of the present invention; Fig. 4 is a cross-sectional view showing a state in which a lens body is provided in the light irradiating body and a light receiving body in the pipetting device according to a fourth embodiment of the present invention; Fig. 5 is an explanatory view showing schematic configuration of a pipetting device according to a fifth embodiment of the present invention; Fig. 6 is an explanatory view showing schematic configuration of a pipetting device according to a sixth embodiment of the present invention; Fig. 7 is an explanatory view showing schematic configuration of a pipetting device according to a seventh embodiment of the present invention; Fig. 8 is an explanatory transverse sectional view showing a level (a surface area) of a liquid to be sucked in a case where it is detected whether a sucked amount of liquid is sufficient or not with the pipetting device according to an eighth embodiment of the present invention; Fig. 9 is an explanatory transverse sectional view showing a

state of the surface of a sucked liquid when contamination of a liquid by foreign matters contained therein is detected with the pipetting device according to a ninth embodiment of the present invention; Fig. 10 is an explanatory view showing a transmission path for a light when a cleaning chip in the pipetting device according to a tenth embodiment of the present invention is empty; and Fig. 11 is an explanatory view showing a transmission path for a light when inside of the cleaning chip in the pipetting device is filled with a cleaning liquid.

BEST MODE FOR CARRYING OUT INVENTION

Detailed description is made for embodiments of the present invention with reference to the related drawings.

Fig. 1 shows schematic configuration of a pipetting device to which the method for sucking/determining a liquid according to the first embodiment of the present invention is applied, and the pipetting device basically comprises a nozzle 2 communicated with and connected to a cylinder 1; an arm 3 for holding the nozzle 2; a drive mechanism 4 for moving the arm 3 upward and downward; a motor 5 for operating the drive mechanism 4; a driving circuit 6 for controlling regular/reverse rotation of the motor 5; and a disposable chip 8 detachably attached to the lower edge section 7 in the nozzle 2.

The nozzle 2 is moved downward at a specified position by the drive mechanism, the liquid level WL is detected by a liquid level detecting mechanism described later, then a liquid 10 such as a serum or a reagent accommodated in a vessel 9 is sucked, and then the pipetting device moves upward to discharge the sucked liquid to another vessel (not shown herein). It should be noted that each of the basic configurations of the pipetting devices according to the present invention is the same as that which is well known so long as a particular mention is not made in the present specification, so that detailed description thereof is omitted herein.

In the nozzle 2, a hole 2a through which a liquid is passed along the longitudinal direction in the center section of the nozzle 2 constructed as same as the nozzle based on the conventional technology is formed, the upper edge section of the hole 2a is communicated with and connected to the cylinder 1, and at the same time in the nozzle 2, the liquid level detecting mechanism comprising a light irradiating body 11 having an optical fiber or a flux of more than two optical fibers and a light receiving body 12 is incorporated, and the lower edge sections of the light irradiating body 11 and of the light receiving body 12 are arranged each in its exposed state in the bottom surface of the lower edge section 7 in the nozzle 2 formed in a reversed convex shape.

Connected to the upper edge section of the light irradiating body 11 is a light emitting section 13 for emitting and supplying a light, the light emitting section 13 supplies a light to a light irradiating body 11, the light irradiated from the lower edge section of the light irradiating body 11 is reflected on the liquid surface WL and is received by the light receiving body 12, then the received and reflected light is converted to a voltage by a photoelectric converting section 14 connected to the upper edge section of the light receiving body 12, a signal for the converted voltage value is sent to an A/D converter 15 for converting it to a digital signal, the digital signal from the A/D converter 15 is received by the control section 16 (e.g. microcomputer) for executing a various types of controlling, and the data for a control signal outputted from the control section 16 is displayed on a display means 21 comprising a CRT or the like.

The control section 16 comprises an input interface 17 for receiving a digital data signal from the A/D converter 15; a ROM 18 for storing therein a program required for computing an inputted signal; a CPU 19 for executing a specified computing according to a program stored in the ROM 18; a RAM 20 for temporarily storing therein a result of computing or data; an output interface 22 for outputting a control signal to various objects to be controlled or to the display means 21 in the device; and a timer 23. It should be noted that the CPU 19 previously stores therein, for instance, specified values or predetermined values identifying a reflected state of a light, executes computing and determining such as comparing the specified values or the predetermined values to measured values, and transmits an instruction for driving and controlling each of the mechanisms according to the determination.

Intrusion of a light from outside or leak of a light transmitted through a light irradiating body 11 and a light receiving body 12 can be prevented without fail by cutting off a light with each of light-proof film layers in which the peripheral surface of the nozzle 2 and an internal peripheral surface of the hall 2a, or a peripheral surface of the light irradiating body 11 and the light receiving body 12 are subjected to coloring to black or the like or to mirroring respectively, so that a clear light signal without any noise can be transmitted, which makes it possible to control more smoothly the control section. It is needless to say that each of the lower edge sections of the light irradiating body 11 and light receiving body 12 is formed, for instance, to a convex lens form, and also formed to a form in which the transmitted light is focused to near the opening at a tip section of the disposable chip 8, and the light reflected on the liquid surface enters into the nozzle 2 for being transmitted.

Next, a description is made for operations of detecting a liquid level in the pipetting device constructed as described above.

When liquid level detection is instructed to the control section 16, the control section 16 outputs a control signal to the light emitting section 13, and the light emitting section 13 supplies a light to the light irradiating body 11. A supply of the light is executed continuously or executed by blinking it at certain time intervals. Then, simultaneously when the light is supplied, the control

section 16 also outputs a control signal to the driving circuit 6, and the driving circuit 6 moves the arm 3 downward into the vessel 9 for a liquid with the motor 5. Further, the control section 16 starts moving the arms downward and the timer 23 incorporated therein starts counting.

In association with the downward movement of the arm 3, the light irradiated from the light irradiating body 11 into a disposable chip 8 is, as shown in Fig. 1, irradiated from the opening section 8a at the tip thereof onto a liquid surface WL, and the light reflected on the liquid surface WL enters again from the opening section 8a at the tip thereof into the disposable chip 8 and is, received by the light receiving body 12.

Namely, the light outputted from the opening section 8a at the tip of the disposable chip 8 through the light irradiating body 11 and irradiated to the liquid surface WL, when the opening section 8a at the tip thereof is above the liquid surface, is reflected on the liquid surface WL, or passed under the water, so that the light hardly returns to the opening section 8a at the tip thereof, and for this reason, the amount of a light received by the light receiving body 12 is at a low level.

An amount of a light received by the light receiving body 12 while the disposable chip 8 is moving downward to a certain position is not changed much.

Then, when the disposable chip 8 has moved downward to the certain position, and a light going out from the opening section 8a at the tip thereof through the light irradiating body 11 and irradiated to the liquid surface WL is reflected on the liquid surface WL and again received into the disposable chip 8 from the opening section 8a at the tip thereof, an amount of a light in the disposable chip 8 cut off from the outside environment momentarily becomes at a high level, so that the light amount at that moment is detected, and the detected amount thereof is compared to a specified value or identified as a predetermined value. In this case, a reflected light can be caught at more accurate timing if the cylinder 1 is moved downward while sucking a liquid.

The photoelectric converting section 14 successively converts the change of the light amount during the time described above to a voltage value, and the control section 16 compares the voltage value to the specified value or identifies that as a predetermined value, and immediately terminate the downward movement of the arm 3 and/or the sucking operation by the cylinder 1.

The signal for voltage value obtained as described above is converted to a digital signal with the A/D converter 15, and the fluctuations of the series of voltage can be stored in the control section 16.

The control section 16 measures with the timer 23 a period of time required from start of measurement until a point of time when the maximum voltage value is obtained, and computes a liquid level WL corresponding to a time previously stored therein with the CPU 19. The data as to whether the liquid level WL has been detected or not is displayed on the display means 21 comprising a CRT or the like. In the embodiment, however, description was made for a case where a liquid level was detected by using the timer 23 as an example, but the present invention is not limited to the case described above, and it is possible to detect a liquid level (position for driving) by using, for instance, a well know), pulse or an encoder.

When the liquid level is detected as described above, the control section 16 provides an instruction to the driving circuit 6 to move the arm 3 downward, and the arm 3 descends for the distance instructed by the control section 16 according to the instruction, so that the tip section of the disposable chip 8 is inserted into the liquid 10, and a required amount of the liquid 10 in the vessel 9 for a liquid is sucked into the disposable chip 8 with the cylinder 1 sucking the liquid according to an instruction by the control section 16.

In the pipetting device according to the embodiment, as described above, a momentary specified value or a momentary predetermined value when fluctuation of the amount of received light reflected on the liquid surface in a space section formed by the disposable chip 8 is extremely different can be caught as a noiseless clear signal without being affected by the outside, so that a liquid level can be detected with high-precision, and the nozzle 2 itself is not contacted with the inside surface of the vessel 9 for a liquid, which makes it possible to prevent cross contamination without fail.

It should be noted that, in the first embodiment, description was made for a case where the lower edge section of the light irradiating body 11 is exposed to the lower edge section of the nozzle 2 as an example, but, as described in the second embodiment shown in Fig. 2, the same effect can be obtained even if the lower edge section of the light irradiating body 11 is led to the outside of the nozzle 2, and a light is irradiated from the outside of nozzle 2, is reflected on the liquid surface WL, and the light reflected thereon is received by the light receiving body 12 provided in the lower edge section of the nozzle 2 through the opening section 8a at the tip thereof.

Fig. 3 shows the third embodiment according to the present invention, and in this embodiment, the device can also be constructed so that the lower edge sections of the light irradiating body 11 and the light receiving body 12 are provided in the side section of the lower edge section 7 of the nozzle 2 in the exposed state respectively, and the disposable chip 8 may be formed with a transparent and photoconductive material, and in that case a light irradiated from the light irradiating body 11 passes through the disposable chip 8 and is irradiated to the liquid surface WL through the opening section 8a at the tip of the disposable chip 8, the reflected light again passes through the disposable chip 8, and the amount of the light can be detected with the light receiving body 12.

Fig. 4 shows the fourth embodiment according to the present invention, and in this embodiment, a focusing lenses 24A, 24B are provided each at a positions lower than each of the lower edge sections of the light irradiating body 11 and the light receiving body 12, the light irradiated from the light irradiating body 11 is focused at a point F_1 on the liquid surface WL, so that a brighter reflected light can be caught, and the resolution can further be improved.

The focusing lenses 24A, 24B may be concave lenses or convex lenses, or may be a combination thereof, and also the irradiated light may be focused not only on the point F_1 on the liquid surface, but also a center F_2 of the opening section 8a at the tip of the disposable chip 8, or at a position F_3 slightly above the opening section 8a at the tip of the disposable chip 8 or at any other appropriate position so long as a change in a quantity of received light can accurately be detected. The focusing lenses 24A, 24B may be provided in either one of the light irradiating body 11 or the light receiving body 12, but in the present embodiment, a lens is always provided in the side of the light receiving body 12. However, in the present invention, the focusing lens described above may not always be provided therein, and it is quite possible to detect how high the liquid level WL is even if a light irradiated from the light irradiating body 11 is supplied to the liquid surface without focusing the light thereon.

On the external and internal peripheral surfaces of the chip nozzle 8 shown in Fig. 4, light-proof film layers 25, 26 each subjected to a coloring to black or mirroring are formed respectively. By forming the light-proof film layers 25, 26 each on the external peripheral surface as well as on the internal peripheral surface of the disposable chip 8, intrusion of a light from the outside into the chip and a leak of a light transmitted therethrough can be prevented without fail, so that a clear light signal without any noise can be received with the light receiving body 12, and a control can more smoothly be provided.

Fig. 5 shows configuration of a nozzle section in a pipetting device according to a fifth embodiment of the present invention, and the embodiment shows a case where the light receiving body 12 is provided at the center of the nozzle 2, and outside the light receiving body 12 a ring-shaped light irradiating body 11 is provided at a specified gap therefrom, and the ring-shaped gap formed between the light irradiating body 11 and light receiving body 12 is communicated with and connected to the cylinder 1 as a suction hole K, and other configuration and effects thereof other than those described above are the same as those in the first embodiment, so that the same reference numerals used in the first embodiment are assigned to the portions corresponding thereto in the figure and detailed description thereof is omitted herein.

Fig. 6 shows a pipetting device according to a sixth embodiment of the present invention, and the embodiment shows a case where the invention is applied to a pipetting device for pipetting, for instance, a reagent or other liquid accommodated in a bottle 30, in which the light receiving body 12 is provided at the center of the nozzle 2, the light irradiating body 11 formed in a ring shape is provided outside the light receiving body 12, and a suction hole K for sucking the liquid in the bottle 30 is provided outside the light irradiating body 11, and other configuration and effects thereof other than those described above are the same as those in the first embodiment, that the same reference numerals used in the first embodiment are assigned to the portions corresponding thereto in the figure and detailed description thereof is omitted herein.

Fig. 7 shows a seventh embodiment of the present invention, and in this embodiment, the same configuration in the nozzle side is formed as that in the third embodiment, and a light is irradiated from the outside of a colored or transparent vessel 9 for a liquid or of a rack 27 in which the vessel 9 is vertically provided, an amount of a light or change of color (a light wave length) reflected on the surface of the liquid 10 is detected through the liquid 10 accommodated in the vessel 9 for a liquid. It should be noted that detection according to color as described above can also be executed in the configuration of the first embodiment.

As described above, like in a case where a light amount is detected, a position of a liquid level WL can be detected even if a change of a light wavelength (color) is detected by the light receiving body 12.

By constructing the device so that color can be detected as described above therein, in a case where two colors of liquid in the vessel 9 for a liquid, for instance, "a blood serum and a blood clot" or "a blood serum, a blood coagulant, and a blood clot" are separated to a layered state by centrifugation and accommodated therein, an interface between a blood serum and other substances can be detected according to a change of the color thereof by slowly moving down the disposable chip 8, which makes it possible to prevent contamination of the chip and a blood coagulant or a blood clot effectively and without fail.

Fig. 8 shows an eighth embodiment of the present invention, and in this embodiment, determination can easily be made as to whether an sucked amount of a liquid is sufficient or not by detecting a reflected area of the liquid 10 or a difference of the reflection height sucked into the disposable chip 8 according to increase/decrease of the light amount.

Fig. 9 shows a ninth embodiment of the present invention, and in this embodiment, in a case where a liquid (blood serum) sucked into a disposable chip 8 is contaminated with foreign matters B such as bubbles or fibrins, a light amount received by the light receiving body 12 varies due to the foreign matters B as compared to that in the normal case, so that successive fluctuations of the light amount due to contamination thereof with the foreign matters B can easily be

detected to determine whether or not the liquid is contaminated with the foreign matters B.

Fig. 10 and Fig. 11 show a tenth embodiment of the present invention, and the embodiment shows a case where an engaging section 32 of the chip 31 in a cleaning system formed to a reversely convex ring shape is formed at the lower edge section of the nozzle 2, the lower edge sections of the light irradiating body 11 and light receiving body 12 are exposed each to the inside of the engaging section 32, and a light irradiated from the light irradiating body 11 can be engaged in the engaging section 32 of the nozzle 2 and received by the light receiving body 12 through the chip 31 in a cleaning system formed with a transparent material, and other configuration and effects thereof other than those described above are substantially the same as those in the first embodiment, so that the same reference numerals used in the first embodiment are assigned to the portions corresponding thereto in the figure, and detailed description thereof is omitted herein.

When the chip 31 in a cleaning system is detachably attached to the nozzle 2 as described above, and in a case where inside of the chip 31 is "empty" as shown in Fig. 10, a light irradiated from the light irradiating body 11 passes through the chip 31 to the opening section at the chip 31 in a cleaning system, again passes through the chip 31 in a cleaning system therefrom to the light receiving body 12, and is received thereby, so that determination can be made as to whether the chip 31 is "empty (exhausted state)" or not by previously measuring an amount of received light in this step.

When inside of the chip 31 is in a state of "filled with a cleaning water" as shown in Fig. 11, a light irradiated from the light irradiating body 11 passes through the cleaning water from the chip 31, again passes through the chip 31 in a cleaning system, and is received by the light receiving body 12, so that determination can be made as to whether the chip 31 is in a state of "filled with a cleaning water" or not by previously measuring an amount of received light in this step.

However, in the embodiments shown in Fig. 10 and Fig. 11, the outer surface of the chip 31 in a cleaning system should preferably be subjected to the same light-proof processing, because detecting conditions are not affected from outside of the chip 31, so that the detection thereof with higher precision can be executed.

As described above, in the present invention, assuming a case where sucking/determining a liquid on a liquid level are executed by using a light, a nozzle is used as a light receiving body, which makes it possible to detect a level of a liquid sucked by the nozzle, without being affected by any measuring conditions outside the chip, and in addition the light receiving body is provided in the nozzle, which makes it possible to prevent without fail generation of cross contamination caused by contacting the light receiving body with a liquid.

In the present invention, not only the liquid level is detected, but also a liquid is filled in the disposable chip or the chip in a cleaning system detachably attached to the nozzle, a light is passed through the liquid in the disposable chip or the chip in a cleaning system, and fluctuation of a light amount of the sucked liquid is detected, so that, for instance, a sucked amount of the liquid, transparency thereof, contamination by bubbles therein, clogging and a state when water has been exhausted are determined.

Furthermore, in the present invention, fluctuation of a light wave length can be detected and a change of color is checked by the nozzle, whereby a liquid level can also be detected.

In the present invention, the color change can be detected according to the nozzle to detect a color of the colored vessel accommodating a liquid therein through the liquid, or according to the nozzle to detect a color of a rack or a color of a holder in which a transparent vessel accommodating a liquid therein is vertically provided, through the liquid, which makes it possible to detect a liquid level corresponding to a change of color environment outside of the disposable chip.

With the present invention, a color of a blood clot or a blood coagulant can be identified in a process in which the nozzle is moving downward while sucking a blood serum, so that an interface on which layers are separated can easily be detected.

In the present invention, the light is not limited to a case of a light which is directly received from the disposable chip or from the opening section of the tip in the chip in a cleaning system attached to the nozzle, and, for instance, a light may be irradiated or received through a transparent disposable chip or a chip in a cleaning system.

In this case, an external surface and/or an internal surface of the disposable chip or the chip in a cleaning system except a portion for transmitting a light is coated with a black film or a mirror film, or the chip is subjected to a light-proof processing such as coloring, whereby fluctuations of the light can be detected with high sensitivity and accuracy.

In the present invention, the nozzle itself is formed with a light transmitting material in a tubular form, and a light irradiating section and a light receiving section are formed in the nozzle formed with the light transparent material, or only the lower edge section thereof is formed with the light transparent material, or optical fibers are provided therein, so that a liquid level can be detected with high-precision without any restriction of liquid sucking operations by the nozzle.

With the present invention, the light receiving edge section of the optical fibers is provided in the bottom surface or the side section of the nozzle, so that a reflected light entering into the disposable chip can be caught without fail. It is needless to say that the nozzle is desirably subjected to a light-proof processing.

In the present invention, lights supplied from the light irradiating body are not necessarily focused, but depending on conditions such as a form or a length of a

chip, a diameter of an opening section, and a light-proof property or the like, a lens body focused at a point where the change of the amount of received light can be checked with high-precision, at the tip of a disposable chip or a chip in a cleaning system, said point located, for instance, at an internal opening section at the tip of disposable chip or at a position slightly lower from a lower edge of the disposable chip, and in this case, a liquid level can be detected with high-precision without any noise therein.

In the present invention, a light is supplied to a liquid accommodated in a vessel by transmitting it continuously through a nozzle or blinking it in a flash therethrough or by means of the optical filters, or is supplied from the outside of the nozzle.

Data obtained by the method for sucking/determining a liquid having the construction as described above is used as data for controlling a pipetting device in which driving required for pipetting a liquid to cylinders for moving upward/downward the nozzle as well as for sucking/discharging a liquid is controlled, which makes it possible to realize a high-precision control.

INDUSTRIAL APPLICABILITY

As described above, the method for sucking/determining a liquid according to the present invention and a pipetting device driven and controlled according to the method are applicable to using for works such as qualifying, quantifying, separating, and pipetting a specimen or a sample, identifying a liquid level, and checking whether contents of pipetting is satisfied or not each in a clinical inspection. In addition, it is applicable to using for works such as qualifying, quantifying, separating, and pipetting a used drug, identifying a liquid level, and checking whether contents of pipetting is satisfied or not each in a chemical analysis, for works such as qualifying, quantifying, separating, and pipetting a specimen and a sample, identifying a liquid level, and checking whether contents of pipetting is satisfied or not each in a DNA analysis, for works such as qualifying, quantifying, separating, and pipetting a used drug, identifying a liquid level, and checking whether contents of pipetting is satisfied or not each in a system of producing drugs, for works such as qualifying, quantifying, separating, and pipetting a specimen and a sample, identifying a liquid level, and checking whether contents of pipetting is satisfied or not each in a bacteria and virus inspection, for works such as qualifying, quantifying, separating, and pipetting a specimen and a sample, identifying a liquid level, and checking whether contents of pipetting is satisfied or not each in a water quality inspection, and furthermore for works such as qualifying, quantifying, separating, and pipetting a used drug, identifying a liquid level, and checking whether contents of pipetting is satisfied or not each in color synthesis.

Claims

1. A method for sucking/determining a liquid, wherein fluctuation of a light obtained from a liquid accommodated in a vessel is detected by a nozzle for sucking the liquid.

2. A method for sucking/determining a liquid according to claim 1, wherein a disposable chip or a chip in a cleaning system is attached to the lower edge section of said nozzle, and said nozzle receives fluctuation of a light around an opening section at a tip of said disposable chip or the chip in a cleaning system.

3. A method for sucking/determining a liquid according to claim 2, wherein said nozzle detects a liquid level by detecting a state in which a light reflected from a liquid surface has come into the opening section at the tip of the disposable chip.

4. A method for sucking/determining a liquid according to claim 1, wherein a liquid is filled in a disposable chip or a chip in a cleaning system detachably attached to said nozzle, and a light is received by said nozzle through a liquid in said disposable chip or said chip in a cleaning system.

5. A method for sucking/determining a liquid according to claim 4, wherein said nozzle determines a sucking rate of a liquid, transparency, contamination thereof with a bubble, and a clogged state or a water-exhausted state of a chip by detecting fluctuation of a light amount of the sucked liquid.

6. A method for sucking/determining a liquid according to any of claim 4 to claim 5, wherein said nozzle recognizes a change of color by detecting a change of a light wave length.

7. A method for sucking/determining a liquid according to any of claim 4 to claim 6, wherein said nozzle detects a color of a colored vessel accommodating a liquid therein through the liquid.

8. A method for sucking/determining a liquid according to any of claim 4 to claim 6, wherein said nozzle detects a color of a rack or a holder, in which a transparent vessel accommodating a liquid therein is provided in the upright state, through the liquid.

9. A method for sucking/determining a liquid according to any of claim 4 to claim 8, wherein said nozzle detects an interface with a solid surface or a liquid surface contacting the bottom surface of the sucked liquid by determining a change of a light amount or a light wave length in a state where said disposable chip is sucking the liquid.

10. A method for sucking/determining a liquid according to any of claim 1 to claim 9, wherein said light is transferred through the disposable chip or the chip in a cleaning system detachably connected to said nozzle.

11. A method for sucking/determining a liquid according to claim 10, wherein an outer surface of said disposable chip or said chip in a cleaning system is subjected to a light-proof processing.

12. A method for sucking/determining a liquid according to claim 11, wherein said light-proof processing is a coloring processing subjected to an outer surface of said disposable chip or chip in a cleaning system and effective to a light-proof processing.

13. A method for sucking/determining a liquid according to any of claim 1 to claim 12, wherein said nozzle is formed with a light transmitting material in a tubular form.

14. A method for sucking/determining a liquid according to any of claim 1 to claim 12, wherein at least a lower edge section of said nozzle is formed with a light transmitting material.

15. A method for sucking/determining a liquid according to any of claim 1 to claim 12, wherein an optical fiber is provided in said nozzle.

16. A method for sucking/determining a liquid according to claim 15, wherein a light receiving edge section of said optical fiber is provided in a bottom surface or a side section of said nozzle.

17. A method for sucking/determining a liquid according to any of claim 1 to claim 16, wherein said nozzle is subjected to a light-proof processing.

18. A method for sucking/determining a liquid according to any of claim 1 to claim 17, wherein a lens body focused at a position where fluctuations of an amount of the received light around the tip section of the chip-can be recognized with high precision, is provided in said nozzle.

19. A method for sucking/determining a liquid according to any of claim 1 to claim 18, wherein a supply of a light to said liquid is executed through the nozzle formed with said light transmitting material.

20. A method for sucking/determining a liquid according to any of claim 1 to claim 18, wherein a supply, reception, and transmission of a light to said liquid is executed through a fiber for a light irradiating or a light receiving fiber provided in said nozzle.

21. A method for sucking/determining a liquid according to any of claim 1 to claim 18, wherein a supply of a light to said liquid is executed from outside of said nozzle.

22. A pipetting device, in which driving required for pipetting a liquid to cylinders for moving upward/downward said nozzle as well as for sucking/discharging a liquid is controlled according to data value obtained by the method for sucking/determining a liquid according to any of said claims 1 to 21.

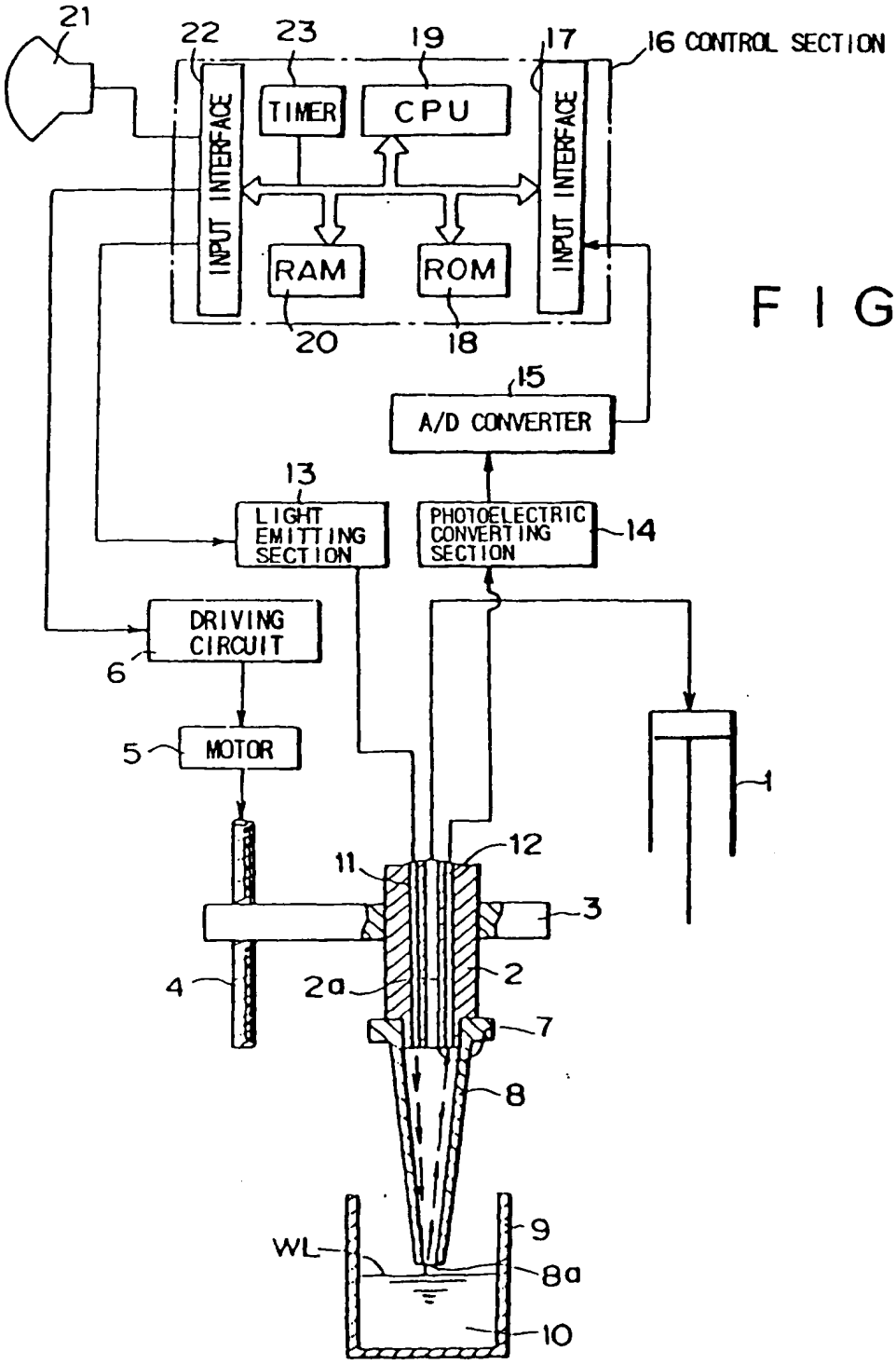


FIG. 1

FIG. 2

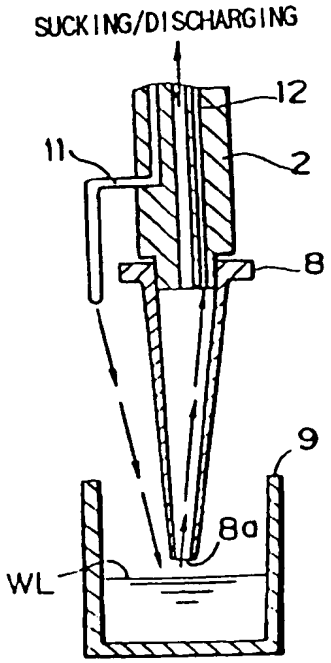


FIG. 3

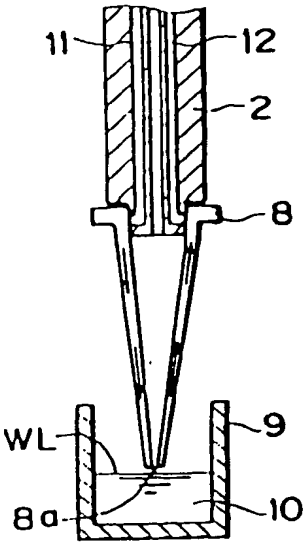


FIG. 4

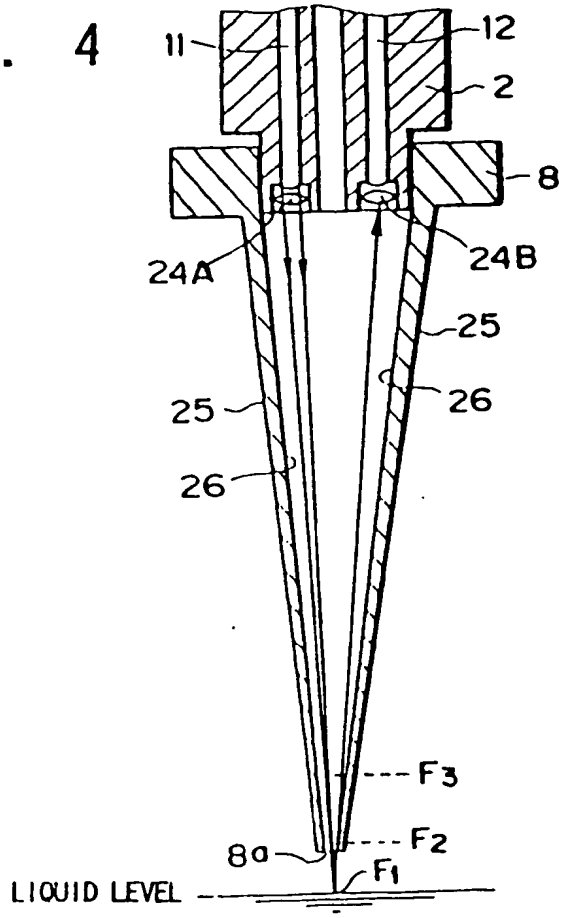


FIG. 5

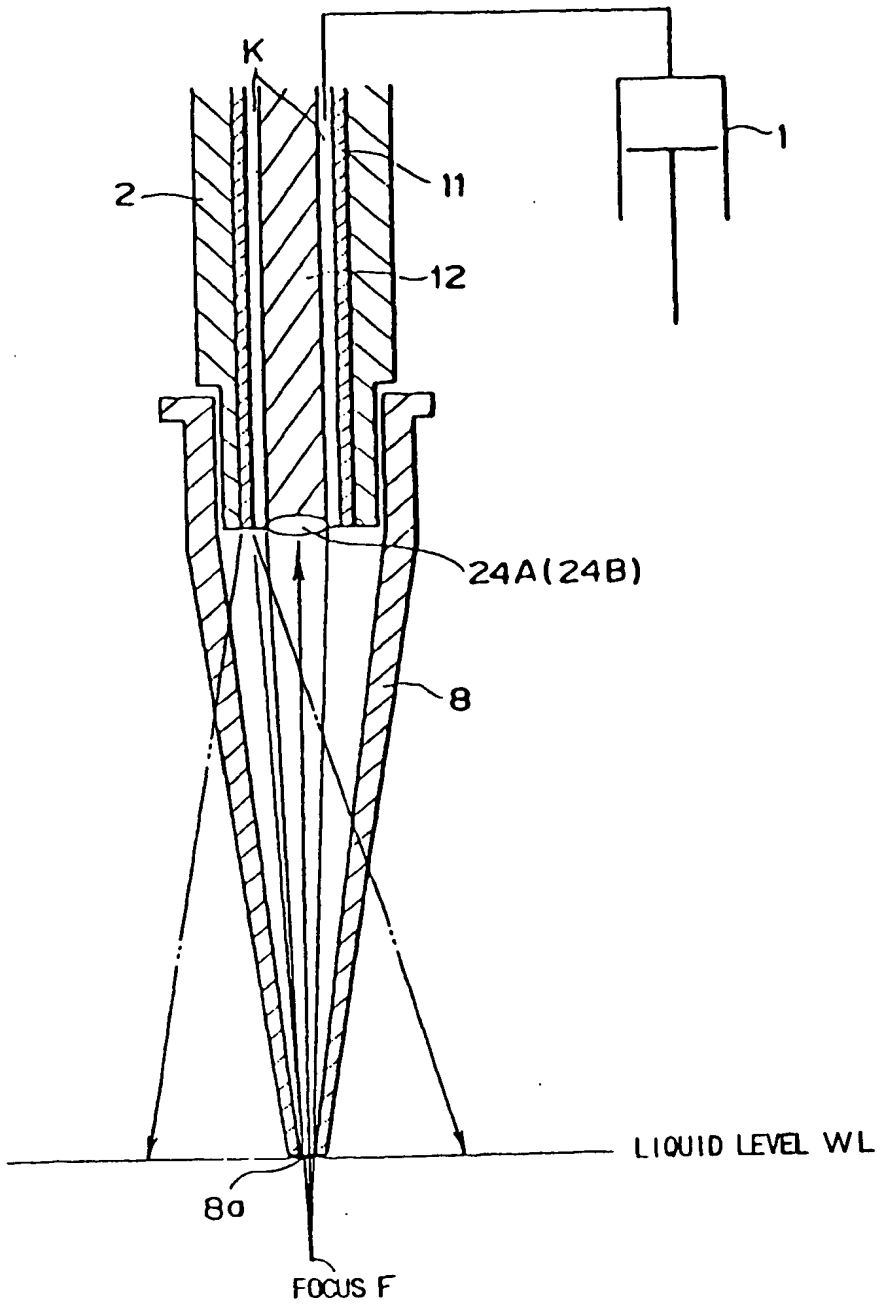


FIG. 6

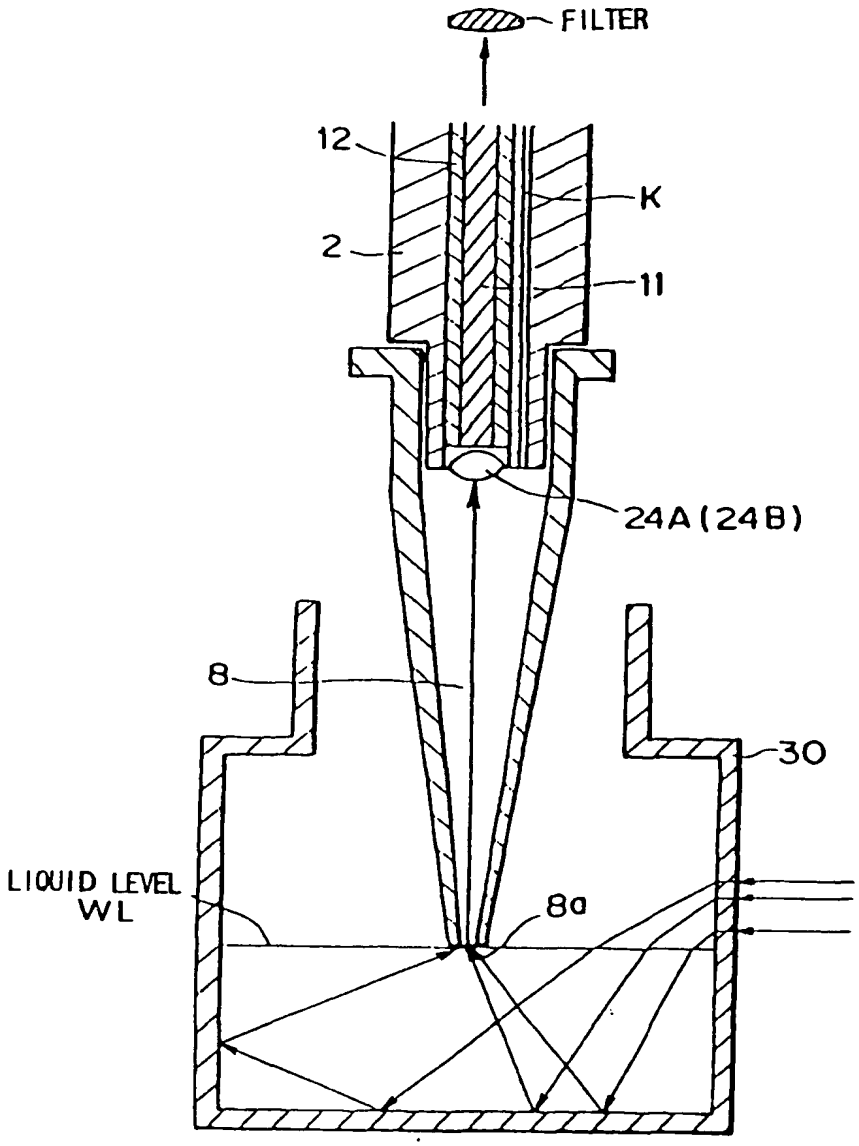


FIG. 7

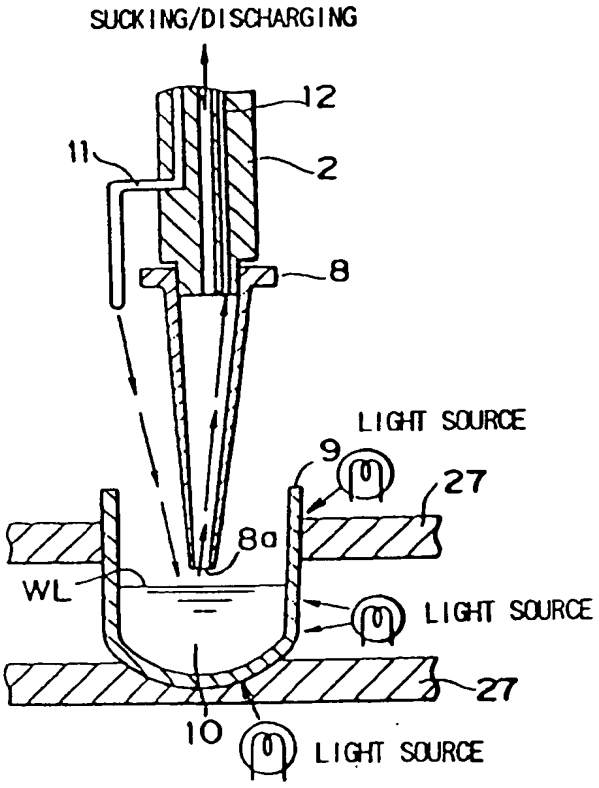


FIG. 8

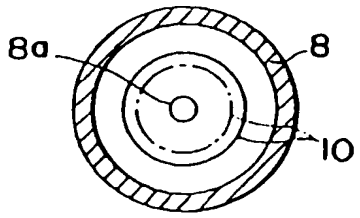


FIG. 9

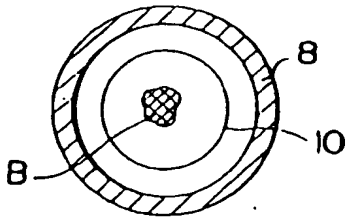


FIG. 10

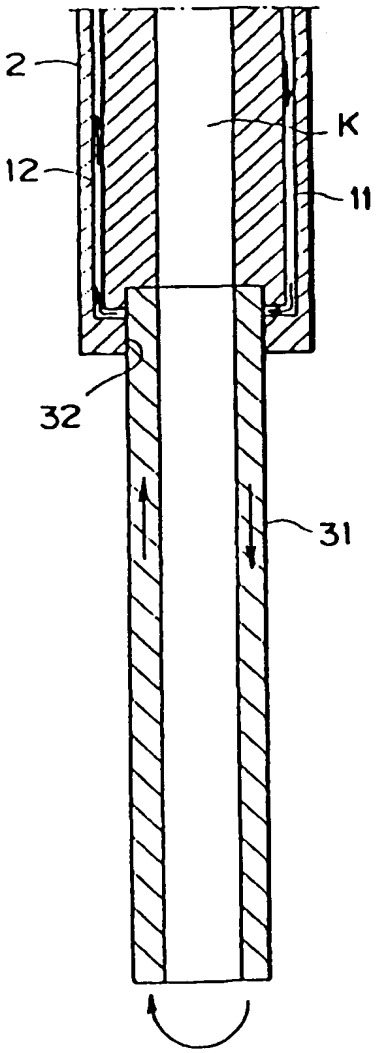
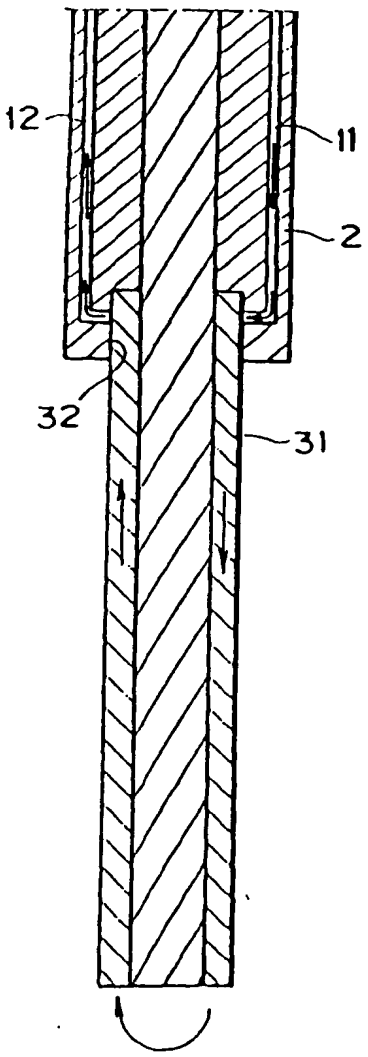


FIG. 11



INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP96/00993

A. CLASSIFICATION OF SUBJECT MATTER
G01N35/06, G01F23/28
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
G01N35/00-35/08, G01N1/00-1/20, G01F23/28

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Jitsuyo Shinan Koho	1926 - 1994
Kokai Jitsuyo Shinan Koho	1971 - 1994
Toroku Jitsuyo Shinan Koho	1995 - 1996

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	JP, 04-204136, A (Tosoh Corp.), July 24, 1992 (24. 07. 92) Claims 1 to 9, Figs. 1 to 5 (Family: none)	1-6, 9-10, 22 11-21
Y	JP, 03-246423, A (K.K. Marushima Aquasystem), November 1, 1991 (01. 11. 91), Fig. 1 and the explanation thereof (Family: none)	11 - 21
Y	JP, 06-191501, A (Oval Corp.), July 12, 1994 (12. 07. 94), Paragraph (0009), Figs. 1a, 1b (Family: none)	11 - 21
Y	JP, 04-84729, A (Shimadzu Corp.), March 18, 1992 (18. 03. 92), Line 20, upper right column to line 10, lower left column, page 4, Fig. 6 (Family: none)	11 - 22
Y	JP, 61-254833, A (Tosoh Corp.), November 12, 1986 (12. 11. 86), Lines 11 to 17, lower left column, page 2	18

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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Date of the actual completion of the international search July 5, 1996 (05. 07. 96)	Date of mailing of the international search report July 23, 1996 (23. 07. 96)
Name and mailing address of the ISA/ Japanese Patent Office Facsimile No.	Authorized officer Telephone No.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP96/00993

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	(Family: none)	

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